REMARKS

This response addresses the issues raised by the Examiner in the Office Action mailed June 14, 2007.

Reply to 35 U.S.C. § 103 Rejection

The Examiner rejected currently pending claims 40-43, 45-69, 71-82 and 119-128, in light of Hudis et al. '99 combined with Henderson et al. and Winer et al., under 35 U.S.C. § 103(a). Applicant respectfully overcomes this rejection for the following reasons.

Hudis et al. '99 discloses a sequential and dose-dense treatment regimen for breast cancer consisting of 3 cycles of doxorubicin 90 mg/m^2, followed by 3 cycles of paclitaxel 250 mg/m^2, and finally 3 cycles of cyclophosphamide 3 g/m^2. Page 93, abstract.

According to the M.P.E.P., "it is improper to combine references where the references teach away from their combination." *See* Section 2145, citing *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). As demonstrated below, Hudis et al. '99 expressly teaches away from the lower dosage regimens disclosed in Henderson et al. and the specification.

First, Hudis et al. '99 expressly teaches away from the well-tolerated dosage of paclitaxel claimed in the instant application. Specifically, Hudis et al. '99 states that "for advanced disease, there seems to be an advantage for 175 mg/m^2 compared with the 135 mg/m^2 when it is administered over 3 hours, *and even higher doses may offer a small additional benefit.*" Page 98, col. 1, first paragraph. Accordingly, with respect to paclitaxel, Hudis et al. '99 concludes that "*[w]ith no confirmation that lower doses and 3-hour infusions were equivalent to higher doses and longer infusions, and on the basis of the earlier clinical trials of paclitaxel*, we chose to use the latter in this pilot trial." *Id.*

Indeed, in reaching the conclusion that higher, and not lower, doses of paclitaxel are superior, Hudis et al. '99 cites Winer et al.--one of the "earlier clinical trials." *See id.*

Second, Hudis et al. '99 expressly teaches away from the well-tolerated dosages of the instant invention when it ultimately concludes that "[d]ose-dense therapy using sequential doxorubicin, paclitaxel, and cyclophosphamide *at escalated doses* is feasible and associated with a promising disease free survival." Page 99, col. II, first full paragraph.

Finally, Applicant respectfully disagrees with the Examiner's view that Hudis et al. '99 "determines that dose densification is a superior strategy to dose escalation." Office Action at page 5. In fact, in the portion of Hudis et al. '99 cited by the Examiner, it states that "[s]equential use of single agents also facilitates *dose escalation* by avoiding overlapping toxicities, *which increases the probability of eradicating the drug-sensitive subpopulations*." Page 94, col. I, second full paragraph. Moreover, Hudis et. al '99 clearly reflects the authors' belief at that time that dose escalation plays a critical role in cancer treatment, since the study in Hudis et al. '99 *itself* utilizes dose escalation (in combination with dose density).

For the foregoing reasons, Applicant respectfully submits that currently pending claims 40-43, 45-69, 71-82 and 119-128 are unobvious in light of Hudis et al. '99, Henderson et al. and Winer et al. and requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

Conclusion

In view of the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at

the telephone number provided below. If there are any fees due, please charge any such fees to our deposit account No. 501561 and reference attorney docket number 93580.010100.

Respectfully,

Date: September 14, 2007

By: _____

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